Intervention Based on Monthly Monitoring Decreases Hemodialysis Access Thrombosis

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We randomized 103 patients (68 arteriovenous [AV] fistulas, 35 polytetrafluoroethylene [PTFE] grafts; mean follow-up 197 days) to monthly measurement of access flow (QAT), monthly measurement of static venous pressure (VPS), or no monthly monitoring (control patients) to determine whether access thrombosis would decrease. Patients with access flow <750 cc/min or with static venous pressure ≥ 0.5 were referred for angiography and angioplasty of stenotic lesions ≥ 50%. Six of sixty-two (9.7%) of monthly monitored patients (MM) developed access thrombosis *vs.* 9 of 41 (22%) of control patients ($p < 0.05$). Fewer MM patients developed thrombosis in AV fistulas (2.4% [2 of 42] *vs.* 15.4% [4 of 26] control patients; $p < 0.05$). Monthly monitored patients had fewer thrombotic episodes than control patients (19 *vs.* 125 per 100 patient-years; $p < 0.01$). Thrombosis rates were lowest in patients receiving monthly access flow measurement (5.9 [QAT] *vs.* 30.3 per 100 patient-years [VPS]; $p < 0.05$). In conclusion, intervention based on monthly access flow measurement or static venous pressure decreased hemodialysis access thrombosis. Measurement of access flow tended to result in lower thrombosis rates than after static venous pressure. We believe that monthly access flow measurement will ensure the lowest incidence of thrombosis and decrease the cost of access maintenance. *ASAIO Journal* 1999; 45:147–150.

Hemodialysis access failure remains a leading cause of hospitalization for patients with end-stage renal disease.[1] Previous studies have shown that programs of regular monitoring of dialysis accesses by measurement of access flow,[2,3] measurement of static venous pressure,[4,5] and color flow doppler ultrasound[6,7] can select a subset of patients at high risk of developing future thrombosis. When coupled with a program of elective correction of significant areas of stenosis, the incidence of dialysis access thrombosis can be decreased.[8–12] There are few studies however that compare the efficacy of different monitoring and intervention protocols on decreasing access thrombosis, and the frequency of monitoring required to minimize thrombosis has been inadequately addressed. The purpose of our study was to determine whether monthly monitoring of dialysis accesses would lead to decreased access thrombosis and whether there was any difference in outcome when different monitoring techniques were used.

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Methods

We randomized 103 patients (68 arteriovenous [AV] fistulas, 35 polytetrafluoroethylene [PTFE] grafts) to receive monthly measurement of access flow (QAT) (Group 1), monthly measurement of static venous pressure (VPS) (Group 2), or no monthly monitoring (control patients; Group 3).

Group1 (QAT). Access flow was measured monthly using the Transonic hemodialysis monitor (Transonic Systems, Ithica, NY) as previously described.[13,14] Patients with access flow measurements <750 cc/min were referred for angiography with subsequent angioplasty of stenotic lesions ≥ 50% in diameter. Group 1 patients also received color flow doppler ultrasound every 6 months as described below.

Group 2 (VPS). Static venous pressure was measured using the modified technique of Besarab *et al.*[5] Static venous pressure was measured at zero blood flow and calculated as VPS = (drip chamber pressure + 17)/systolic BP. All patients were dialyzed using Fresenius 2008H machines (Fresenius USA Inc., Walnut Creek, CA). Patients with static venous pressure ratios ≥ 0.5 were referred for angiography with subsequent angioplasty of stenotic lesions ≥ 50% in diameter. Group 2 patients also received a color flow doppler ultrasound every 6 months.

Group 1 and Group 2 patients were combined for analysis to form the group of monthly monitored patients (MM).

Group 3 (control patients). These patients received no monthly monitoring. Color flow doppler ultrasounds were performed on control patients every 6 months.

Ultrasound Protocol

Color flow duplex ultrasounds were performed on all patients every 6 months. Real-time imaging was performed using a Phillips SD800 machine (Philips Medical Systems, Irvine, CA). Imaging was performed for the total access, arterial anastomosis, venous anastomosis, and native run-off to the subclavian vein. As part of the ultrasound study, access flow volume was measured using a Hewlett Packard Sonos 100 machine (Hewlett Packard, Andover, MA). Access flow was calculated by multiplying the time-averaged velocity by the cross sectional area of the access. Accesses with ≥ 50% stenosis, low access flow (≤ 800 ml/min in PTFE grafts or ≤ 600 ml/min in AV fistulas), or a ≥ 25% decline in flow compared with a prior study were referred for angiography with possible angioplasty. All patients were dialyzed using Fresenius 2008H machines.

Episodes of thrombosis, angioplasty, surgical revision, pharmacomechanical thrombolysis, and surgical thrombectomy were maintained in an on-going database. For the purpose of this study, primary patency was defined as remaining patent

Table 1. Patient Demographics

	No. of patients	Patient age	% Diabetic	% AV fistulas	Access age (days)	Follow-up (days)
Control (Group 3)	40	59.7	30	65	851.7	204.5
Monthly monitoring (Group 1 and Group 2)	63	55.7	25.8	66.1	542.8	192.6
		ns	ns	ns	$p < 0.05$	ns

AV, arteriovenous.

without thrombosis throughout the study period. Total thrombosis rates were defined as the total number of thromboses including repeated episodes of clotting expressed as rates per 100 patient-years.

Statistical analysis was performed using GBSTAT for Windows, Version 6.01 (Dynamic Microsystems Inc., Silver Spring, MD). Categorical variables were analyzed using Chi-square. Continuous variables were analyzed using Anova with protected t-tests and nonparametric statistics, including the extended median test and Kolmogorov Smirkow two sample test.

Results

One hundred and three patients were entered into the study protocol. The study group was comprised of 68 AV fistulas and 35 PTFE grafts. Patient demographics were similar in both groups with the exception that the age of the patient's vascular access at entry to the study was greater in control patients (Group 3) (**Table 1**). This was true for both AV fistulas and PTFE grafts (**Table 2**). The mean age of the patients was 59.5 years. The mean follow-up was 197 days.

Six of sixty-two (9.7%) patients who underwent monthly monitoring (Groups 1 and 2) developed an access thrombosis, compared with nine of forty-one (22%) control patients ($p < 0.05$). There was no significant difference in the development of a single thrombosis between the two groups of monthly monitored patients (2 of 27 [QAT] *vs.* 4 of 35 [VPS] NS) (**Table 3**).

Two of forty-two (2.4%) monthly monitored AV fistulas developed a thrombosis, compared with four of twenty-six (15.4%) in the control patient group ($p < 0.05$). Although fewer patients developed an access thrombosis in PTFE grafts monitored monthly, this was not statistically significant (20%, 4 of 20 [MM] *vs.* 33.3%, 5 of 15 [control patients]; NS). There were no significant differences between the QAT and VPS groups in the development of a first thrombosis in either AV fistulas or PTFE grafts (**Table 3**).

When repeated episodes of thrombosis were included, monthly monitored patients had fewer total episodes of thrombosis than the control patient group (19 *vs.* 125 per 100 patient-years; $p < 0.01$). Comparison of the monitoring techniques revealed that patients monitored with monthly access flow measurements had a lower incidence of thrombosis than those patients followed with monthly static venous pressures (5.9 [QAT] *vs.* 30.3 thrombosis per 100 patient-years [VPS]; $p < 0.01$) (**Table 4**).

Arteriovenous fistulas followed with monthly monitoring had a lower total thrombosis rate than control patients (16.8 *vs.* 27.1 per 100 patient-years; $p < 0.05$). Polytetrafluoroethylene grafts receiving monthly monitoring had fewer total episodes of thrombosis than control patients (23.2 [MM] *vs.* 246.7 per 100 patient-years [control patients]; $p < 0.01$) (**Table 4**).

Comparison of the different monthly monitoring techniques revealed that although both methods of monthly monitoring resulted in less thrombosis than the control patient group, thrombosis rates were lowest in patients followed with monthly access flow measurement (5.9 [QAT] *vs.* 30.3 thrombosis per 100 patient-years [VPS]; $p < 0.05$). Although QAT patients had lower thrombosis rates than VPS patients in both AV fistulas and PTFE grafts, these differences were not statistically significant.

Table 2. Comparison of Access Age*

	All accesses	PTFE grafts	AV fistulas
Control (Group 3)	851.7	800.3	881.4
Monthly monitoring (Groups 1 and 2)	542.8	464.6	582
Control *vs.* MM	$p < 0.05$	$p < 0.05$	$p < 0.05$
QAT (Group 1)	542.6	435.4	593.4
VPS (Group 2)	543	486.4	572.5
QAT *vs.* VPS	ns	ns	ns

* In days.

PTFE, polytetrafluoroethylene; AV, arteriovenous; MM, monthly monitored patients; QAT, access flow; VPS, static venous pressure.

Table 3. Primary Patency During Study Period

	All accesses		AV fistulas		PTFE grafts	
	Thrombosed	Patent	Thrombosed	Patent	Thrombosed	Patent
Control (Group 3)	9	32	4	22	5	10
MM	6	56	2	40	4	16
Control *vs.* MM		$p < 0.05$		$p < 0.05$	ns	ns
QAT (Group 1)	2	25	1	18	1	7
VPS (Group 2)	4	31	1	22	3	9
QAT *vs.* VPS	ns	ns	ns	ns	ns	ns

MM, monthly monitoring; QAT, access flow; VPS, static venous pressure; AV, arteriovenous; PTFE, polytetrafluoroethylene.

Table 4. Total Thrombosis Rate Expressed as Rate per 100 Patient-Years

	All accesses	AV fistulas	PTFE grafts
Control	125	27.1	246.7
MM	19	16.8	23.2
	$p < 0.01$	$p < 0.05$	$p < 0.01$

MM, monthly monitoring; AV, arteriovenous; PTFE, polytetrafluoroethylene.

The number of angioplasties were similar in both study groups. A total of 18 angioplasties were performed (10 monthly monitoring, 8 control; NS). Only two patients received angioplasties resulting from Doppler ultrasound studies (one patient from Group 1 and one from Group 2). Additionally, after thrombosis, only one new access was placed (Group 3) during the study period.

The mean age of accesses that thrombosed was lower than in accesses that remained patent (375 *vs.* 705 days; $p < 0.01$). A higher percentage of diabetic patients developed thrombosis (25%, 7 of 21) than nondiabetic patients (2.9%, 1 of 35) ($p < 0.05$).

Discussion

Hemodialysis access failure continues to be one of the leading causes of hospitalization for patients with end-stage renal disease. During the past 10 years, there has been mounting evidence that monitoring of hemodialysis access by measurement of static[15] or dynamic venous pressures,[16] access flow,[14,17] or color flow doppler ultrasound[6,18–22] can select a subset of patients at increased risk of future access thrombosis. When coupled with correction of significant areas of stenosis either by angioplasty or surgery, the incidence of hemodialysis failure can be decreased.[5,7,11,12,15] For these reasons, the recent Dialysis Outcomes Quality Initiatives (DOQI)[23] report recommends regular monitoring of access function in all hemodialysis patients. There is, however, limited data on the frequency of monitoring required to minimize access thrombosis and little data available comparing the efficacy of different monitoring techniques. Additionally, most studies have focused only on PTFE grafts and have not evaluated the efficacy of monitoring in AV fistulas.

This pilot study shows that a program of intervention guided by monthly monitoring either by measurement of access flow or measurement of static venous pressures coupled with semi-annual color flow duplex ultrasounds decreased access thrombosis in both AV fistulas and PTFE grafts. This improvement in outcome was most evident when repeated episodes of thrombosis and intervention were included.

The thrombosis rates achieved in monthly monitored patients (19 per 100 patient-years) were low by historical standards. Even in PTFE grafts, monthly monitored patients had a thrombosis rate of only 23.2 per 100 patient-years. This rate approaches the rates achieved in patients with AV fistulas and is within DOQI guidelines.

Although intervention based on monthly access flow measurements resulted in lower thrombosis rates in both native AV fistulas and PTFE grafts than did measurement of static venous pressure, the small number of patients and the low thrombosis rates made it impossible to adequately separate these groups. Future trials incorporating much larger numbers of patients, beginning from the time of access placement, will be necessary to determine which combination of monitoring techniques will minimize access thrombosis and the costs of access maintenance.

Our study had several limitations. Access flow and static venous pressure were monitored monthly. Whether more frequent monitoring is beneficial can therefore not be determined. We used the same intervention criteria for both AV fistulas and PTFE grafts. Artereovenous fistulas have lower static venous pressures than PTFE grafts and remain patent at lower flow rates.[20] However, no clear pressure or flow criteria for fistulas exist. Our criteria for intervention was based upon changes in flow, but not changes in pressure. This may limit the efficacy of pressure monitoring. Lastly, accesses in the control patient group were older than those in the monthly monitoring group. Bay *et al.*[24] has shown that older accesses had less tendency to clot than new accesses. In our data, one would expect that the control group would tend to have less thrombosis. This, however, was not the case.

The role of duplex ultrasound cannot be established by this study. Before this study, we had a successful ultrasound based access management program and believed it would be unethical to replace this program until data were available to show that an alternative monitoring program was equally effective. Besarab *et al.*[15] previously showed improved outcomes when color flow duplex ultrasounds were added to a program of monitoring static venous pressures. Further studies are necessary to evaluate whether measurement of access flow alone is as efficacious as a combined program of baseline and semi-annual ultrasound coupled with monthly access flow measurement.

Conclusion

In conclusion, intervention based on monthly monitoring of access flow or static venous pressure appeared to decrease the incidence of hemodialysis access thrombosis. Measurement of access flow appeared to result in lower thrombosis rates than after static venous pressures. We believe that a program of monthly measurement of hemodialysis access flow coupled with semi-annual color flow duplex ultrasounds should be instituted to ensure the lowest incidence of hemodialysis access thrombosis, hospitalization, and cost associated with hemodialysis access maintenance.

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